REMARKS

A. Status of the Claims

Claims 1-37 were pending at the time of the Action. Claims 16-33 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 5, and 34-37 have been canceled. Claims 1, 6, and 11-15 have been amended. New claims 38-53 have been added. Thus, claims 1-4, 6-15, 38-53 are currently under examination.

No new matter has been added by the amendments. Support for the term "lysate" can be found in the specification at page 3, paragraph [0010]. Support for the recitation "wherein the number of antigen-presenting cells is greater than the number of cells represented in the lysate" can be found in the specification at page 44, paragraph [0153]. Paragraph [0153] teaches that while previous reports using a co-culturing technique used a ratio of 1 antigen-presenting cell for each tumor cell in the lysate, or 1 antigen-presenting cell per 3 tumor cells in the lysate, the methods of the present invention permitted the use of lysate from fewer cells. Support for static electroporation and flow electroporation can be found in the specification at paragraph [0081].

B. The Rejections Under 35 U.S.C. § 102

1. The Claims Are Novel Over Duke

Claims 1-3, 5, 6, 8-15, and 34-37 stand rejected under § 102(a) as anticipated by Duke (WO 02/39951). Applicants traverse this rejection.

The current claims are directed to a method for loading an antigen-presenting cell with one or more antigens, comprising: preparing a mixture comprising antigen-presenting cells and a lysate of a hyperproliferative cell, a microorganism-infected cell or a microorganism, wherein the number of antigen-presenting cells is greater than the number of cells represented in the lysate; and electroporating the mixture in a manner sufficient to load the one or more antigens

into the antigen-presenting cells. The Action has not established that Duke teaches every element of the claims.

In particular, the Action has not established that Duke teaches the preparation of a mixture comprising antigen-presenting cells and a lysate of a hyperproliferative cell, a microorganism-infected cell or a microorganism, wherein the number of antigen-presenting cells is greater than the number of cells represented in the lysate. As discussed in the present specification, typical methods of loading an antigen-presenting cell (APC) required at least an equal ratio of APCs to lysed cells, if not an excess of lysed cells to prime a CTL response (*see e.g.,* Specification, p. 44, ¶ [0153]). Similarly, Duke teaches using an excess of yeast vehicle to load DCs. Duke discloses DC to yeast vehicle ratios of 1:5, 1:10, 1:20, 1:40, and 1:100 (*see e.g.,* FIGs. 2A, 2B, 3A, and 3B), and states that increasing the yeast to DC ratio increases the antigen specific T cell proliferation (p. 34, ln27-28). Accordingly, Duke does not appear to teach a method in which it is the APCs that are in excess. Furthermore, Duke actually appears to teach away from such a method by stating that increasing the yeast to DC ratio increases the antigen specific T cell proliferation.

For at least the reasons described above, the current claims are novel over Duke. Applicants, therefore, request the withdrawal of the rejection.

2. The Claims Are Novel Over Scott-Taylor

Claims 1-2, 8, 10, 34, and 37 stand rejected under § 102(b) as being anticipated by Scott-Taylor. Applicants traverse this rejection.

The Action states that Scott-Taylor discloses the fusion of MCF-7 and LNCaP tumor cells with DCs by application of an electric current. Such a method, however, does not teach all of the elements of the current claims. The presently claimed invention requires the step of

preparing a mixture comprising antigen-presenting cells and ***a lysate*** of a hyperproliferative cell, a microorganism-infected cell or a microorganism. The Action has not established that Scott-Taylor teaches preparing a mixture comprising antigen-presenting cells and a lysate.

The presently claimed invention also requires that the number of antigen-presenting cells be greater than the number of cells represented in the lysate. As mentioned above, Scott-Taylor does not teach the use of a lysate. However, even if Scott-Taylor did teach the use of a lysate, it would still fail to teach a method where the number of antigen-presenting cells is greater than the number of cells represented in the lysate. Scott-Taylor appears only to teach the fusion of equal numbers of DCs and tumor cells (*see*, p. 267, col 2).

For at least the reasons described above, the current claims are novel over Scott-Taylor. Applicants, therefore, request the withdrawal of the rejection.

3. The Claims Are Novel Over Kugler

Claims 1-2, 8, 10, and 34-37 stand rejected under § 102(b) as being anticipated by Kugler. Applicants traverse this rejection.

The Action states that Kugler discloses the electrofusion of dendritic cells with renal tumor cells. As discussed above in regard Scott-Taylor, such a method does not teach all of the elements of the current claims. The presently claimed invention requires the step of preparing a mixture comprising antigen-presenting cells and ***a lysate*** of a hyperproliferative cell, a microorganism-infected cell or a microorganism. The Action has not established that Kugler teaches preparing a mixture comprising antigen-presenting cells and a lysate.

The presently claimed invention also requires that the number of antigen-presenting cells be greater than the number of cells represented in the lysate. As mentioned above, Kugler does not teach the use of a lysate. However, even if Kugler did teach the use of a lysate, it would still

fail to teach a method where the number of antigen-presenting cells is greater than the number of cells represented in the lysate. Kugler appears only to teach the fusion of equal numbers of DCs and tumor cells (*see*, p. 333, col. 1).

For the reasons provided above, the current claims are novel over Kugler. Applicants, therefore, request the withdrawal of the rejection.

C. The Rejection Under 35 U.S.C. § 103

Claims 1-2, 4-8, 10, 11, and 13-15 stand rejected under § 103(a) as unpatentable over Asavaroengchai in view of Kim or Chen, and further in view of Spetz. Applicants traverse this rejection.

The combination of Asavaroengchai, Kim, Chen, and Spetz fails to teach or suggest every element of the current claims. As discussed above, the presently claimed invention requires that the number of antigen-presenting cells be greater than the number of cells (*e.g.*, tumor cells) represented in the lysate. Asavaroengchai teaches the use of 3 tumor cells for each DC. Thus, the method taught by Asavaroengchai requires more than 3 times the number of tumor cells. Kim and Chen disclose the loading of APCs by electroporation with only a single antigen, OVA. Kim and Chen do not mention, much less provide any guidance as to the amount of cell lysate that should be used to load APCs by electroporation. Thus, combining Kim and Chen with Asavaroengchai fails to teach that the number of antigen-presenting cells be greater than the number of cells (*e.g.*, tumor cells) represented in the lysate. Spetz appears to teach only the use of virally infected splenocytes and thus, provides no guidance regarding electroporation or ratios of APCs to lysed cells.

The present invention provides surprising and unexpected results that one of ordinary skill in the art could not have predicted based on the cited references. As taught by the present

specification, the assumed low concentration of, for example, a tumor-associated antigen in a whole tumor lysate required that a considerable amount of tumor lysate be used per APC in co-incubation methods. p. 24, ¶ [0086]. Prior to the teachings of the present invention, typical ratios of whole-tumor lysate to DCs used in co-incubation studies was 1:1 (*i.e.* one tumor cell in the tumor tissue used to make the lysate per dendritic cell to which the whole tumor lysate was added) or in some cases (*e.g.*, the Asavaroengchai reference) the ratio was 1:3, *i.e.*, even more whole-tumor lysate must be prepared to load a desired number of DCs. *See* Specification, p. 24, ¶ 0086. Accordingly, such methods required large amounts of source material for the preparation of the cell lysate. Obtaining such large amounts of source material may be impossible during early stages of disease when only a small number of cells are affected. *See* p. 9, ¶ [0032].

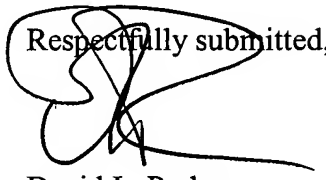
In contrast, the present invention provides methods that require substantially less source material for the preparation of the cell lysate. For example, the studies described in Example 8 and FIG. 3 show that the APCs loaded with tumor cell lysate according to the method of the present invention elicited a T cell response more than 2-fold greater using 1/10 the amount of tumor cells than APCs loaded by co-incubation. Such a result would not have been expected based on the references cited in the Action.

For at least these reasons, the current claims are patentable over Asavaroengchai, Kim, Chen, and Spetz. Applicants, therefore, request the withdrawal of this rejection.

D. Conclusion

Applicants respectfully submit that the claims are in condition for allowance. The Examiner is invited to contact the undersigned Attorney at (512) 536-3055 with any questions, comments, or suggestions relating to this patent application.

Respectfully submitted,



David L. Parker
Reg. No. 32,165
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 536-3055 (telephone)
(512) 536-4598 (facsimile)

Date: July 29, 2005